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14. ABSTRACT

This report results from a contract tasking Lhasa Limited as follows: The contractor will investigate techniques to apply computational methodologies and biotechnology database information to predicting the possible toxicity of chemicals. The goal is to combine available information on chemical structures and biotoxicity to predict toxicity of a chemical from its structure. Routes of entry into the body, organs and systems affected, biological half life, modes of inactivation, and dose-response relationships will be part of the prediction. In addition, the contractor's system will provide "missing data" flags. As such, the system will indicate what information, if provided, would allow a more accurate prediction to be established. The method can be used to predict effects of foreseeable industrial and environmental chemicals as well as unforeseen exposures during military operations.

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BICTP End of Project Report

The final software deliverable, prototype software D4, has been despatched to Kevin Geiss at Wright Patterson Air Force Base (WPAFB).

As had been agreed, this project was merged with a complementary one funded by Pfizer Inc and the deliverable provides the features that were specified for both projects. These include being able to link DEREK for Windows to a variety of types of external models. The purpose of the WPAFB project was to link to external databases: the delivered prototype includes a demonstration link to a copy of the Gold carcinogenicity database in Access, allowing rules to be written based on its contents.

One requirement given in the original outline document for the joint project is absent from the prototype software. It was a requirement for rule writers to be able to specify hierarchies of external models and it was not implemented after further consideration because it was found to be inappropriate: it would make use of the system more complicated for rule writers to use, to little or no advantage in practice.

All other specific requirements that were outlined for the combined project have been met:

1 Rule-writers can refer to external models;
2 Whether external models are used is controlled by user option settings;
3 The system can provide a list of available external models;
4 Data from external models and used by reasoning rules is displayed to the user;
5 Whether external models are used is recorded in rtf reports;
6 New words like “My_Program_Value”, to be used by rule writers, can be declared and associated with specific external models;
7 The system continues automatically without data from an external model if the model does not respond within a reasonable time;
8 If an external model is unavailable, rules return ‘open’;
9 The system works both interactively and with command line processing;
10 The Adaptor, which is the result of this project, is designed to allow programmers or systems staff at user sites to create their own links to novel external models;
11 The system can deal with external models which have security features such as passwords (through appropriate design of the associated external adaptors);
12 The system reports confidence levels if external models return them.

P N Judson
26th March 2004

Adaptor User Guide

Contents

Chapter 1. Introduction

This user guide describes how to use the LPS_Adaptor application. The LPS_Adaptor is a version of LHASA Limited's LPS program that allows Physico-Chemical Property values derived from applications outside of LPS to be taken into account during processing. Previous versions of DEREK for Windows were able to take into account Physico-Chemical Properties such as Log Kp and molecular weight, however the LPS_Adaptor application provides a mechanism by which any number of further Physico-Chemical Properties can be considered. This mechanism has been designed so that it is user-extensible thus allowing users to write rules that make use of in-house or proprietary, calculation or modelling packages. Note that these changes do not apply to the METEOR component of LPS.

1.1 References

This document should be read in conjunction with the LPS 6 User guides,

- *DEREK for Windows* and
- *DEREK for Windows Knowledge Base Editor.*

Administrators and advanced users may also wish to read *Using the Adaptor Manager Administration Utility*.
Information about writing custom Adaptors can be found in the document *How to write Adaptors for LPS.*

1.2 Installation and licensing.

For installation instructions see the documents *Installing LPS_Adaptor* or *Administering LPS_Adaptor*.

The features of the program described in this document are protected by licensing and an "Adaptor" licence is required in order to use them.

1.3 Overview

Several stages are involved in giving Derek for Windows the ability to make use of Physico-Chemical Properties that will be calculated by External Models.

1. The Physico-Chemical Property must be defined in the DEREK for Windows knowledgebase by creating a Physico-Chemical Property Record.
2. Absolute Reasoning Rules must be written which make use of these Physico-Chemical Properties.
3. The relevant External Model must be installed either locally or on a machine that is running the adaptor host service.
4. An Adaptor must be written (or otherwise obtained) to allow LPS to communicate with the External Model. For details about how to do this refer to the document *How to write Adaptors for LPS.*
5. The stand-alone Adaptor Manager Administration Utility must be used in order to create an Adaptor Lookup File, this tells LPS where to look for the External Model. For further details, see the user guide *Using the Adaptor Manager Administration Utility*.
6. Switch on the use of this feature in LPS by setting the processing constraints.
7. Process a query chemical structure.

These steps may seem a little complicated but they are necessary in order to provide flexibility and extensibility. Steps 1,2,6 and 7 are described later in this document.

1.4 Definitions.

Adaptor	A program file (DLL) that has the ability to communicate with an External Models. An adaptor may handle more than one Physico-Chemical Property. This word is also used more widely due to the fact that this stand of development was called *The Adaptor Project*.
Adaptor Lookup File	The shared document that tells LPS_Adaptor which adaptor and which class in that adaptor provide the functionality to process the requested PCP, and where and how to connect to the adaptor.
External Model	A program, database or application that can calculate or otherwise supply values for Physico-Chemical Properties. External Models will usually be third party applications.
LinkFile.xml	See Adaptor Lookup File.
LPS	A suite of programs developed by LHASA Limited, currently comprising *DEREK for Windows* and *METEOR*. These programs are separately licensed and are available with or without editor access. Note that this user guide often uses the term LPS when LPS_Adaptor would be more accurate.
LPS_Adaptor	The version of LPS that was created by the Adaptor project and which is the subject of this document, as distinct from mainstream LPS (which is currently at version 7). It is expected that LPS and LPS_Adaptor will merge in future.
Physico-Chemical Property	This term is used in a very general sense to include any statistic or value derived from an External Model. Sometimes abbreviated to PCP.
PCP Name	The name used to identify a particular Physico-Chemical Property. It is used by LPS to identify Physico-Chemical Property records and to link these with both Reasoning rules and External Models.

There are further details for many of these terms in the Adaptor Components section below.

1.5 Summary of New Features

The LPS_Adaptor program provides the following new features.

- During processing the program can pass a test structure to an external model to obtain a Physico-Chemical Property value. This value is then taken into account in the *Absolute Reasoning*.
- The program is also able to obtain Physico-Chemical Property values from tagged SD Files, if required. Each method is able to take calculations of tolerance into account.
- A new *Phys-Chem Properties* tab has been added to the processing constraints form to allow the user to control how Physico-Chemical Properties are obtained.

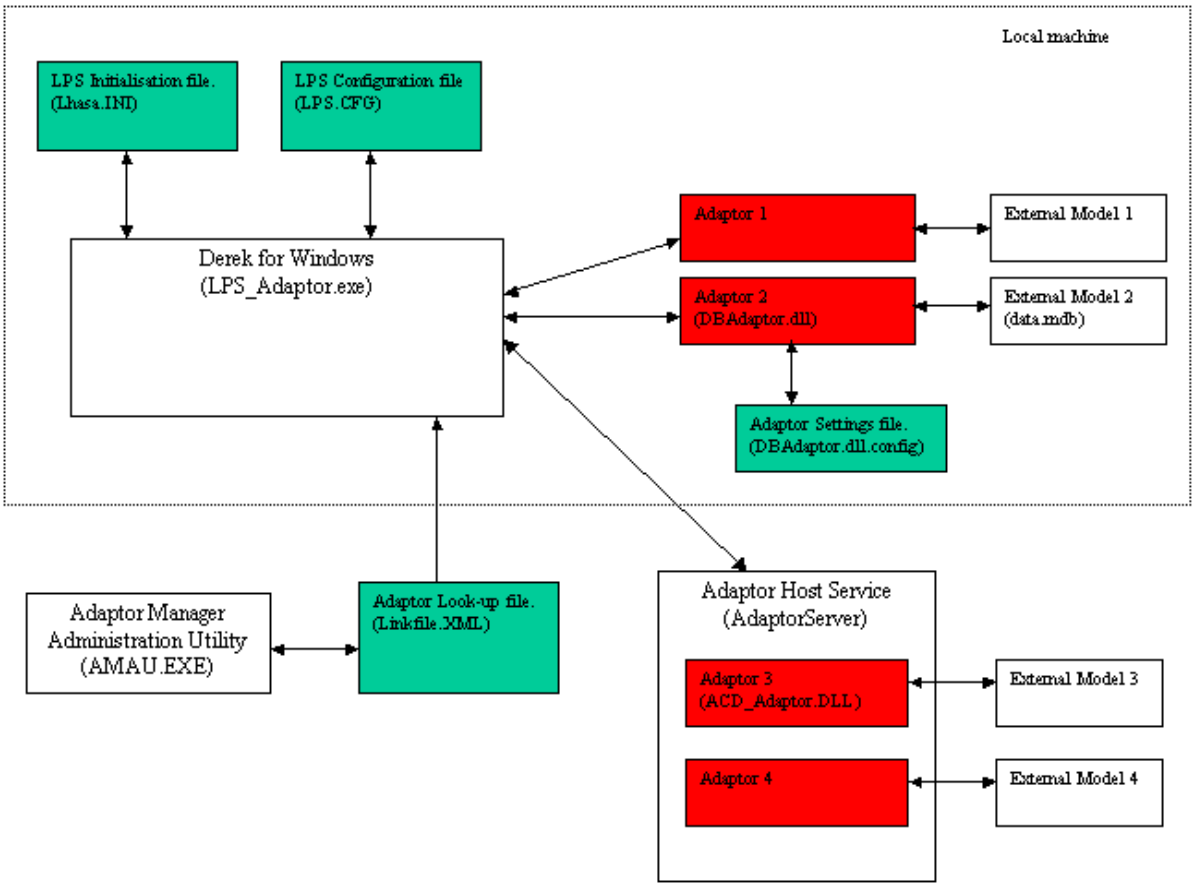
Editor features:

- Ability to write reasoning rules that make use of Physico-Chemical Properties.
- Ability to define Physico-Chemical Property Records.

1.6 Adaptor components

The diagram shows some of the components that may be involved when LPS is using external models. The names in parenthesis show actual filenames for some instances of these components.

Figure 1



The LPS initialisation and configuration files shown on the top left are the usual ones that the LPS program uses.

1.6.1 LPS Initialisation file

The LPS Initialisation file stores the name of the LPS configuration file (usually "LPS.CFG") along with other settings such as directory paths for the "Home" directory etc.

1.6.2 LPS Configuration file

In addition to its traditional roles, the LPS Configuration file now also stores the Adaptor Look-Up path and filename along with the following processing constraint settings:

- The SD File Tag,
- the enabled status for Input from SD file and
- the enabled status for Input from External Models.

NB: It does not store the path to the Adaptor for each Physico-Chemical Property, as these are stored in the Adaptor Lookup File.

1.6.3 Adaptor Look-Up File.

The Adaptor Lookup File contains the path to the Adaptor for each Physico-Chemical Property defined in the knowledgebase. (This path appears on the Physico-Chemical Properties Tab of the processing constraints form under the column heading "External Model".) For remote adaptors this 'path' will be the URL of the Adaptor Host Service including the port number. The Adaptor Lookup File may also contain a class name for each Physico-Chemical Property.

This file can be placed on the local machine or may be placed on a shared area to allow simultaneous use by several LPS users. Its contents, like any xml document, can be viewed in Internet Explorer or can be edited with any text editor, however, changes to the Adaptor Lookup File must conform to the specification defined in the Schema Definition file (Linkfile.XSD) that accompanies the Adaptor Lookup File. For this reason the *Adaptor Manager Administration Utility* should always be used for creating and editing these files. For further information refer to the document *Using the Adaptor Manager Administration Utility*.

1.6.4 Adaptor Manager Administration Utility

The Adaptor Manager Administration Utility (or AMAU) is a stand-alone utility for creating and editing Adaptor Lookup Files. For further information refer to the document *Using the Adaptor Manager Administration Utility*.

1.6.5 Adaptor Host Service

The adaptor host service is a Windows service that allows Adaptors (and their External Models) to be accessed by several users at a time. An installer is provided to independently install the Adaptor Host service, which is required on any machine that will host Adaptors. It appears on the Windows 'Services' utility under the name "AdaptorServer". In a multi-user system, the Adaptor Lookup File can be on a file server accessible by all clients; this will have URL addresses to remote (hosted) adaptors for the PCPs. This helps to ensure that all users of DEREK for Windows use the same Adaptor and External Model for a particular PCP and so ensure consistency of results across users. The adaptor host service automatically scans in subdirectories of the directory in which it is installed, looking for Adaptor DLL files. If any are found, the adaptor host service then attempts to host them.

1.6.6 Adaptor

Adaptors are separate executable files that are specific to each External Model or to a group of related External Models. They can be installed locally or on remote machines (allowing access to shared External Models). It is possible for users to create their own in-house Adaptors that LPS will be able to use. This requires use of Microsoft VB.NET. For more details see "How to write Adaptors for LPS.doc".

1.6.7 Adaptor Settings File

Each Adaptor may (or may not) have an associated settings file to store settings relating to the External Model. For example, the DBAdaptor.xml file stores the path to the access database file, Gold_data.mdb along with information about how the rat and mouse data can be found in this database. The format of these files is determined entirely by the Adaptor and they may differ significantly in the number and type of elements that they contain.

1.6.8 External Model

The External Model may be a database, an executable file or anything else that an Adaptor can communicate with and retrieve information from.

Chapter 2. Writing Rules Using External Models

This Chapter describes how you can write Absolute Reasoning Rules that make use of values derived from sources outside of the LPS program. These may be obtained directly from External models or may have been calculated earlier and supplied to LPS in an SD file. Additionally you can enter these values manually during processing. You can choose between these input methods using the processing constraints form (see "Changing processing constraints for External Models").

For either of these input methods you must write Absolute Reasoning Rules that refer to particular Physico-Chemical Properties and must also define the Physico-Chemical Properties in the DEREK for Windows knowledgebase. These tasks are the subject of this chapter.

2.1 Defining New Physico-Chemical Properties

If you want to refer to a new Physico-Chemical Property in a reasoning rule, you must also define the Physico-Chemical Property by entering a "Physico-Chemical Property Record" into the knowledgebase. This is described in the following sections.

2.1.1 Editing Physico-Chemical Property Records

You can view, edit, add and delete Physico-Chemical Property Records using the **Physico-Chemical Properties** form. This form is displayed using the menu item **Database | Phys-Chem Properties** in the editor.

Figure 2

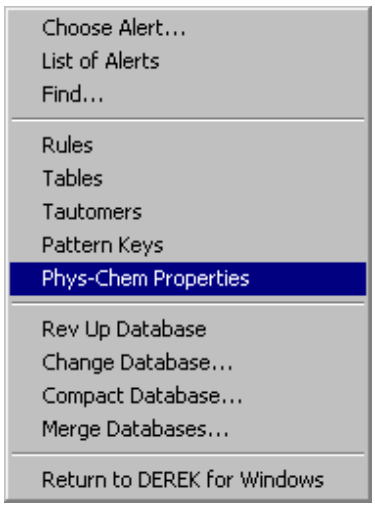
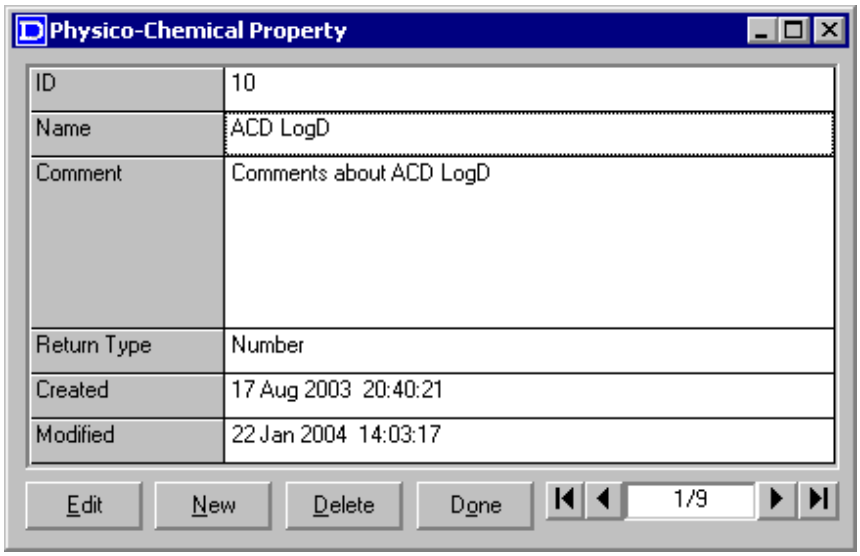


Figure 3



The purpose and usage of the fields is described later in the section "Adding New Physico-Chemical Properties".

Note:

Only users with Lhasa Status are able to alter Lhasa data (denoted as usual by ID numbers below 500000).

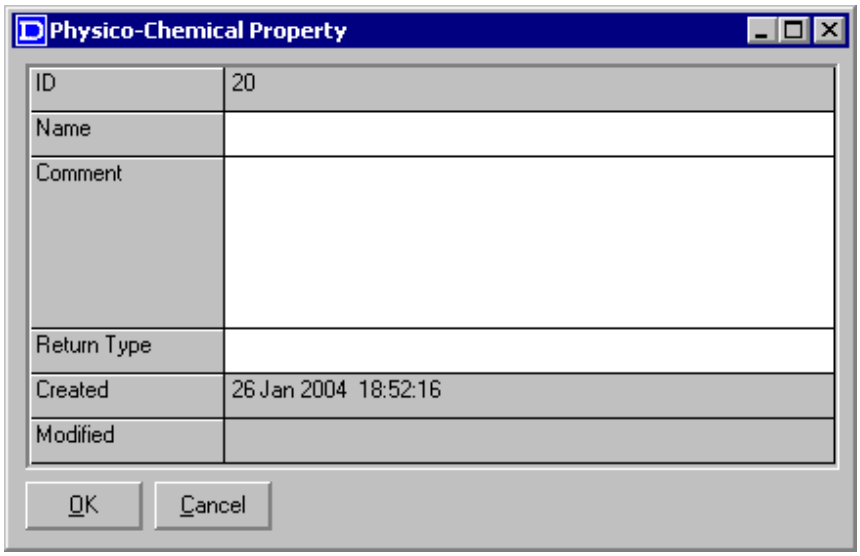
Users cannot delete Physico-Chemical Properties that are "in use". For these purposes, a Physico-Chemical Property is *in use* if there are active Reasoning Rules in the database that refer to it. The *in use* status of a Physico-Chemical Property is not affected by processing constraint settings.

Users can edit Physico-Chemical Properties that are in use but are restricted to editing the **Comment** field only.

2.1.2 Adding New Physico-Chemical Properties

You can add a new Physico-Chemical Property by clicking the **New** button on the Physico-**Chemical Property Form**. A blank record is presented which you can complete. When adding a new record the **Edit**, **New**, **Delete** and **Done** buttons are replaced by **OK** and **Cancel** buttons as shown below.

Figure 4



Enter text into the **Name**, **Comment** and **Return Type** fields, then click **OK** to confirm the new Physico-Chemical Property Record.

2.1.3 Fields on the Physico-Chemical Properties Form.

The **Name** field must be completed and must differ from the names used by existing Physico-Chemical Property Records. It must also differ from any existing **Proposition** value in an Absolute Reasoning Rule. This is to avoid a situation where Absolute Reasoning Rules attempt to set the values of Physico-Chemical Properties directly, rather than obtaining them from an external source.

The **Comment** field is Optional.

The **Return Type** field is used to specify the type of values that the External Model should provide and will be either Number or String

The **ID**, **Created** and **Modified** fields are read-only as these values are generated automatically.

This information forms part of the DEREK for Windows knowledgebase and is stored in the DEREK for Windows Access Database.

2.1.4 Linking to External Models.

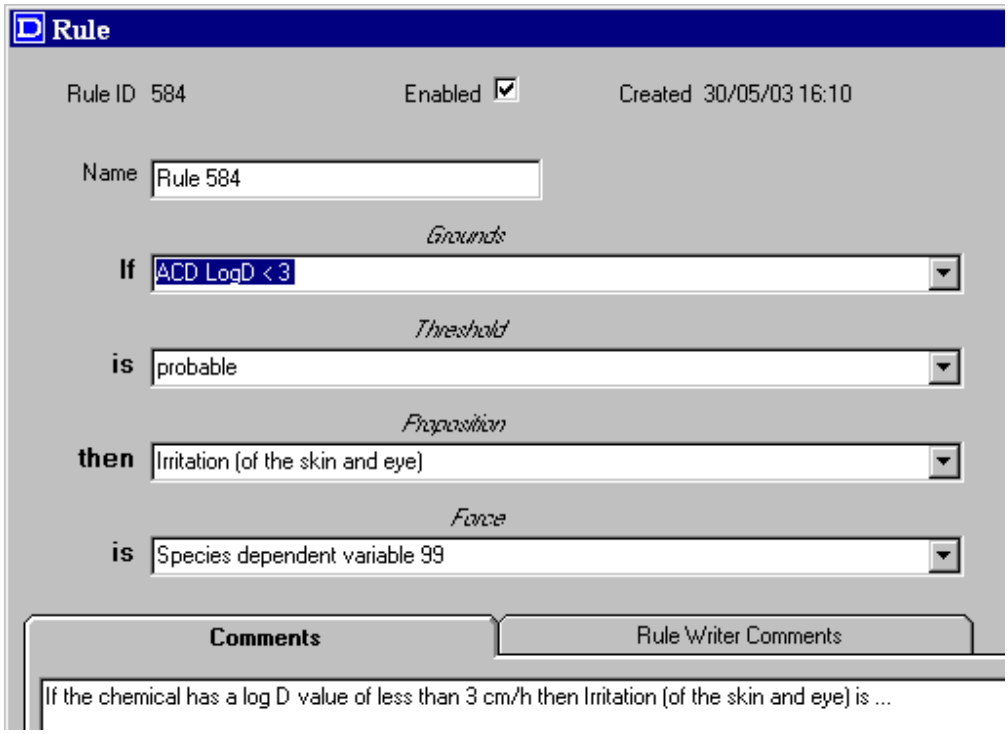
To find out how to accomplish the task of providing a link between the Physico-Chemical Property record and the External Model that will supply this value, refer to the chapter “Changing Processing Constraints for External Models” and the document “Using the Adaptor Manager Administration Utility”

2.2 Absolute Reasoning Rules

External models can be accessed through Absolute Reasoning Rules in the following way:

- Open the DEREK for Windows editor and choose **Database | Rules** in the Derek for Windows Editor. The *Reasoning Window* will open showing the reasoning rules tree.
- Edit an existing rule or add a new one to display the Absolute reasoning rules form.

Figure 5



- To refer to a Physico-Chemical Property you must type its name into the **Grounds** field, followed by an *operator* and a *value*. The figure above shows an example in which the rulewriter wishes to test if the LogD value for the submitted compound is less than 3, as calculated by the "ACD" application.
- The program will check that the entry in the **Grounds** field conforms to the accepted format (see below). If the text fails the checks, an appropriate message will be presented.
- You can complete the rest of the fields and commit the rule in the usual way.

2.2.1 Input Checks – Grounds Field

The Grounds fields will accept input of the form:

Property name operator value

Property name is a string denoting the particular Physico-Chemical Property to be evaluated.

operator can be one of the following:

Numerical Comparison:

<	Less than
<=	Less than or equal
>	Greater than
>=	Greater than or equal
=	Equal
String Comparison:	
IS	Exact match
CONTAINS	Match is found within result
LIKE	Wildcard match using '*' and '?'. '*' will match zero or more characters. '?' matches any single character.

value is some text denoting a value to be compared with the value returned by the External Model.

The system will check that value is of a type which is appropriate for the chosen Physico-Chemical Property (as defined in the Physico-Chemical Property record, see above) and that operator is also appropriate.

If the value is of an incorrect type or the operator is inappropriate for the chosen Physico-Chemical Property, a suitable warning message will be displayed and you will be unable to commit the Rule in an enabled state until the problem has been rectified.

If the Property Name is not known to the program at the time the rule is being written, you will be able to complete the rule but will only be able to commit the rule if the **Enabled** field is not ticked. You will then be free to enter the appropriate Physico-Chemical Property details in a new *Physico-Chemical Property Record*, after which you can return to the rule to enable it.

2.2.2 Input Checks – Proposition Field

The program does not allow reasoning rules where the entry in the **Proposition** field appears to be a Physico-Chemical Property. Specifically, if the proposition contains a Physico-Chemical Property operator ('>', '=', 'IS' etc, see ?) that is surrounded by text other than white space, then it is disallowed. If it starts with a PCP Name (e.g. "Dba-rat Variable") then you will be given a warning but are allowe d to keep this value.

These checks are to stop rulewriters from being able to write rules that attempt to set the values of Physico-Chemical Properties directly. Physico-Chemical Properties can be given values only by the three methods stated in the first paragraph of this Chapter, however the rulewriter can write rules that use these values, possibly to set variables. For example if two Physico-Chemical Properties have been defined, 'dba-rat' and 'dba-mouse', and you wishes to write rules that extrapolate from one to the other, then this should be done using an intermediate variable.

For example the following Rule would be disallowed,

If dba-rat > 5 is certain then dba-mouse > 5 is probable.

And should be written as follows:

If dba-rat > 5 is certain then dba-mouse > 5 variable is probable.

Other Rules can then be written which make use of the variable ‘dba-mouse > 5 variable’.

2.2.3 Viewing rules that refer to External Models

You can view Absolute Reasoning Rules that refer to External Models in the usual way, by selecting **Database | Rules** in the Derek for Windows Editor. The *Reasoning Window* will open and the LHASA reasoning rules tree will be displayed under **LHASA RULES**.

Chapter 3. Changing processing constraints for External Models

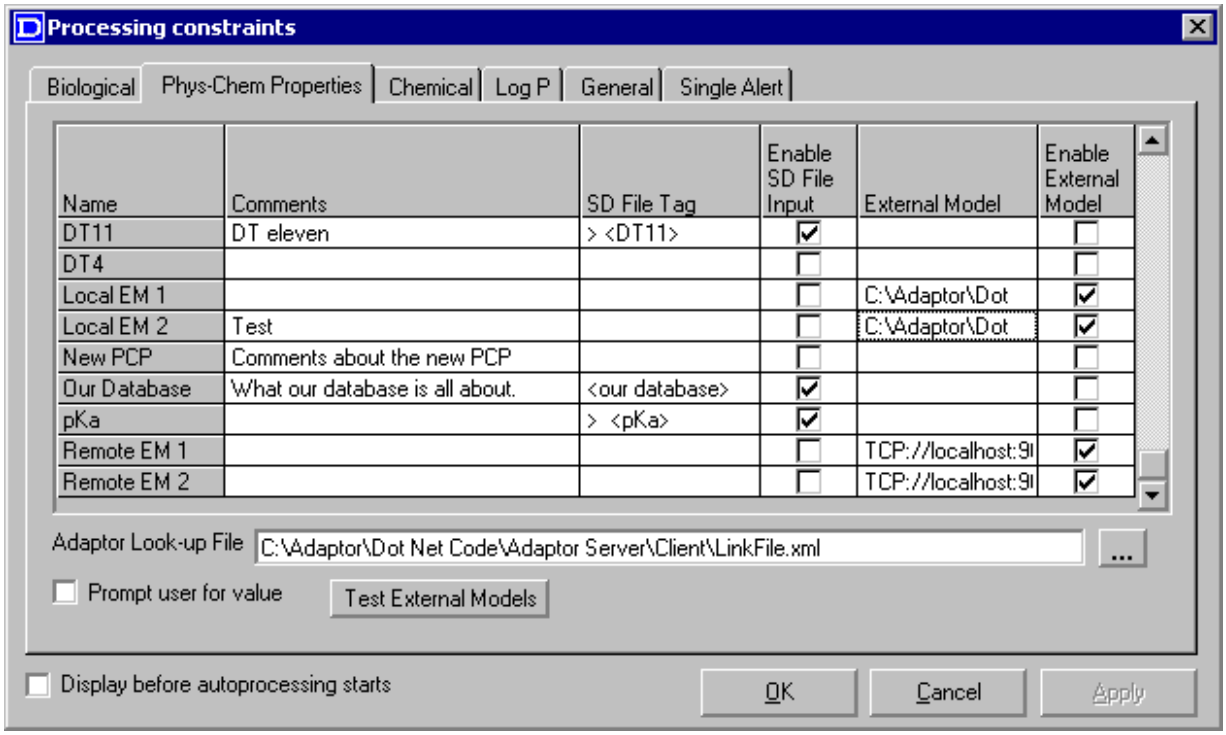
This Chapter describes how you can alter the processing constraints that relate to the use of External Models, Input from SD files and interactive input.

3.1 The Processing Constraints Form

Select **Options | Processing Constraints** to view the Processing Constraints form.

The *Phys-Chem Properties* tab shows a list of Physico-Chemical Property Records that have been entered into the database (see the section "Adding new Physico-chemical properties" in the chapter "Writing Rules that use External Models").

Figure 6



You can view the **Name** and **Comments** of the Physico-Chemical Properties but cannot edit them using this form.

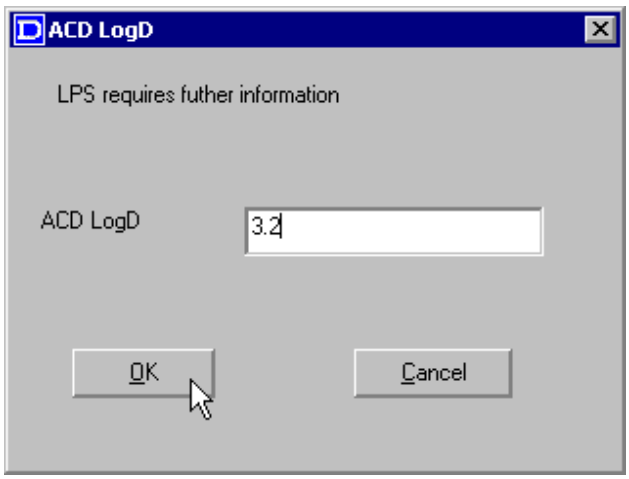
3.1.1 Enabling and disabling different methods of input.

There are two tick box fields for each Physico-Chemical Property, one relating to SD File input and the other to the use of External Models. You can click any of these fields in order to enable or disable it. Input from SD file takes priority so if both fields are ticked, the program will attempt to obtain the Physico-Chemical Property value from the External Model only if it cannot be found in the SD File.

3.1.2 Prompt User for Input

If the tick box field at the bottom of the Physico-Chemical Properties tab is ticked the program will display the 'User Input' form during processing to allow you to enter the Physico-Chemical Property's value interactively.

Figure 7



If both of the tick boxes in the grid are unticked for a particular Physico-Chemical Property, and the "Prompt user for Value" tick box is also unticked, then any rules using that Physico-Chemical Property will not be considered during processing (or, to be precise, they will resolve to "OPEN").

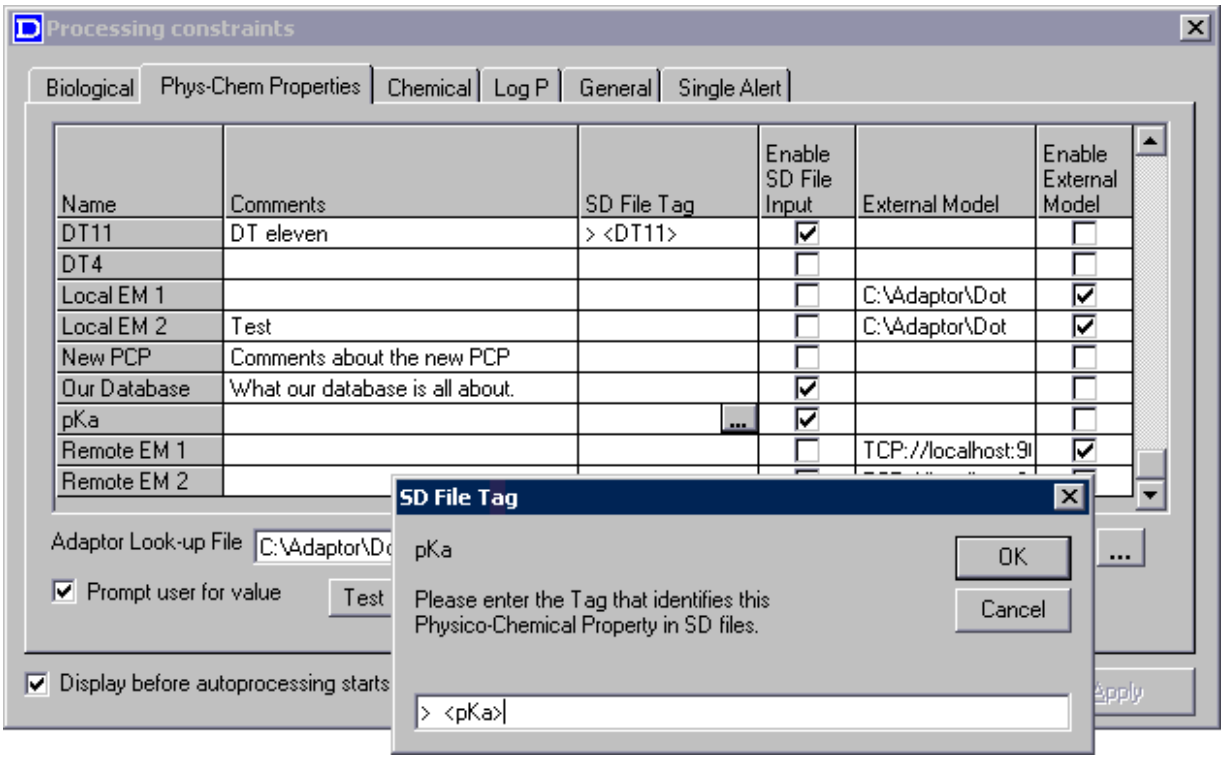
The "User Input" form is not displayed in the following cases:

- If the program manages to obtain the Physico-Chemical Property value from an external model.
- During AutoDerek processing.
- During Command-line processing.
- If there are no active Absolute Reasoning rules that use the particular Physico-Chemical Property.

3.1.3 SD File Input

In order to get a Physico-Chemical Property value from an SD file you must specify the Tag value that identifies this value in the SD File. When you click on an **SD File Tag** field, a small button appears on the right hand side of the field. You can click this button in order to enter a new SD File Tag as shown below. Only one **SD File tag** can be specified for each Physico-Chemical Property. The **SD File Tag** works in the same way as the **Name** field on the **General** Tab; all text on the line following the tag is treated as the Physico-Chemical Property value. The tag can also contain wildcards to allow matching against Tags that include other text on the same line.

Figure 8



3.1.4 Where this information is stored.

The **SD File Tag**, and the two tick box values for each Physico-chemical property are stored in the [Constraints] section of the file *LPS.CFG* with the other processing constraints, however the value in the External Model field is stored in the *Adaptor Lookup File*.

The entries in the LPS.CFG file appear in the format shown below (this is provided for information only as it should never be necessary to edit the LPS.CFG file directly):

```
AdaptorLookUpFile=C:\Program Files\Lhasa Ltd\Lhasa Adaptor Manager\LinkFile.xml
PhysChemProperty(0)=ACD LogD|Disabled|Disabled|ACD LogD
PhysChemProperty(1)=Another LogD|Disabled|Disabled|LogD Lite
PhysChemProperty(2)=dba-mouse|Enabled|Disabled|
PhysChemProperty(3)=dba-rat|Enabled|Disabled|
PhysChemProperty(4)=DT1|Disabled|Enabled|DT1
PhysChemProperty(5)=DT11|Disabled|Enabled|DT11
PhysChemProperty(6)=DT3|Disabled|Disabled|
PhysChemProperty(7)=DT4|Disabled|Disabled|
PhysChemProperty(8)=Our Database|Disabled|Disabled|Database1
```

3.1.5 Obtaining Physico-Chemical Property values from External Models

The value displayed in the **External Model** field is the Path and file name of the specific Adaptor that is used to access the *External Model*. This can be viewed in full as a tooltip if the field is selected. This value can be changed only by using the Adaptor Manager Administration Utility (AMAU).

If you enable input from an External Model where no External Model path has been specified, or if you enable SD file input without specifying an SD File Tag, a suitable message will be presented and you will not be able to apply these changes until the fault is remedied.

If no constraints exist in the LPS.CFG file when the processing form is loaded, the tick boxes will display as grey squares to denote the fact that no constraint setting is stored. This can happen when new Physico-Chemical Properties are entered into the database or if they are renamed. If you click the **OK** or **Apply** buttons without setting the "unknown" tick boxes to an enabled or disabled value, they will default to a disabled status. This means that the grey squares will only be seen once because when the processing constraints form is next opened they will be unticked.

The Physico-Chemical Property entries in the LPS.CFG file are written when the **Apply** button is used or when the processing constraints form is closed using the **OK** button. In this way, redundant Physico-Chemical Property entries (for example those relating to Physico-Chemical Properties that have been deleted from the database) are automatically cleared away from the CFG file.

3.1.6 The External Model Test Button

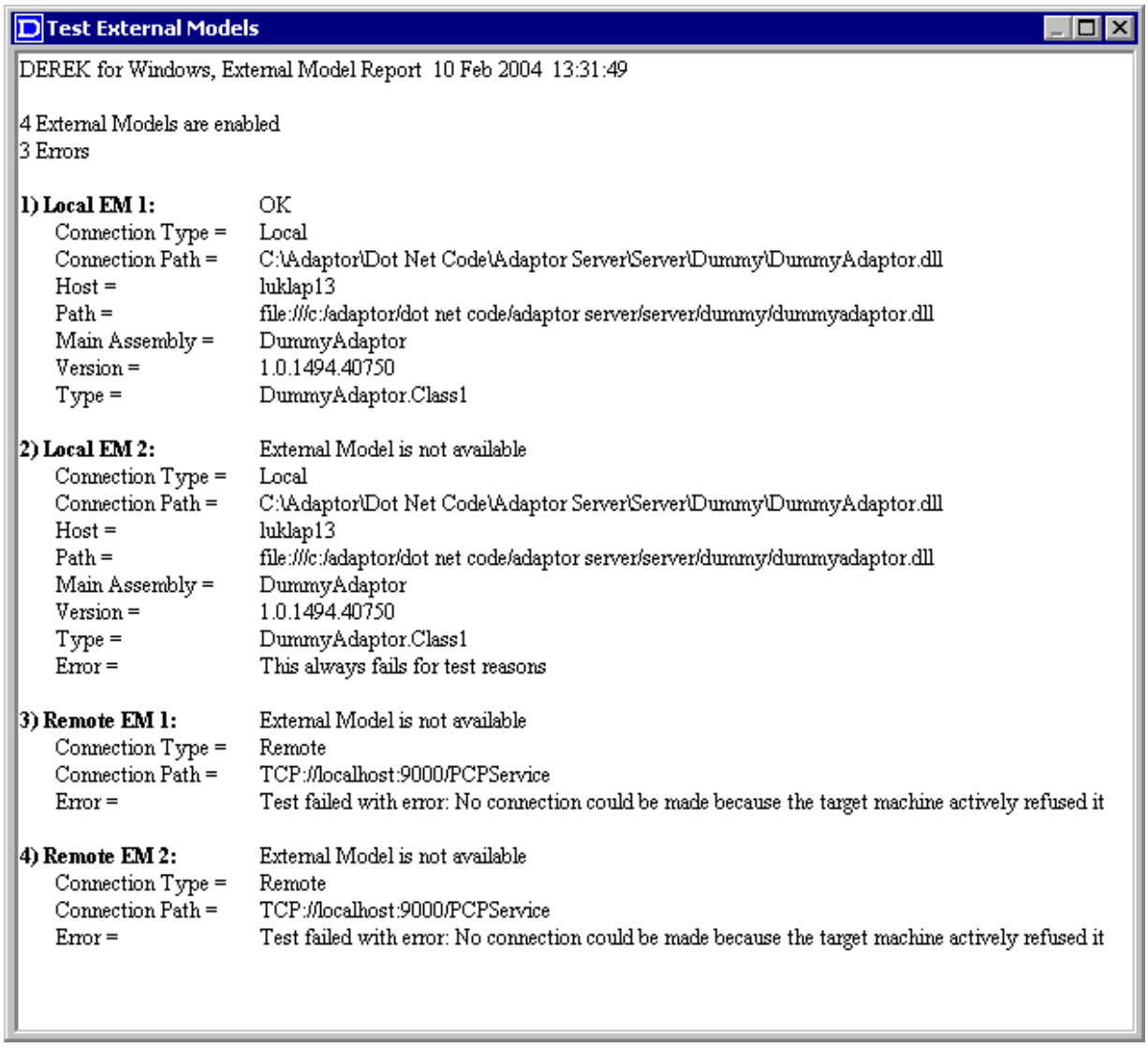
The command button **Test External Models** allows you to check the current state of External Models. The External Model that a Physico-Chemical Property Record uses may exist in a remote location (e.g. on a different computer on a local area network), it is therefore possible that it may be temporarily unavailable due to a network problem or such like.

When the External Model test button is clicked the program produces a report on screen to show the state of the External Models that are enabled in the Physico-Chemical Properties grid. The state will be one of the following three values and is shown next to the Physico-Chemical Property's name.

State	**Meaning**
"OK "	The External Model can be contacted and appears to be working correctly.
"No External Model has been defined for this Physico-Chemical Property"	The Adaptor Lookup File does not contain an entry for this Physico-Chemical Property.
"External Model is not available"	Some other problem has been encountered (see External Model report for further information).

The report also shows further information about each External Model. This information varies for each Physico-Chemical Property and may include information from LPS_Adaptor, the Adaptor or from the External Model itself. If the External Model is not available then further information about the nature of the error will usually be provided in this list. This information is also included in processing reports.

Figure 9



You will be able to apply these processing constraint settings even if there are problems with External Models because the External Model may become available later, prior to processing.

3.1.7 The Adaptor Lookup file

The path and filename of the Adaptor Lookup File is displayed in a text box at the bottom of the form accompanied by a browse button (shown with an ellipsis), which can be used to find an alternate file.

These items are visible whether you have editor status or not. This is to allow users to point to an Adaptor Lookup File that is shared between all users at a client site. Users may also want to specify an alternative Adaptor Lookup File in order to experiment with the use of different External Model settings.

The Adaptor Lookup File can be edited using the Adaptor Manager Administration Utility (AMAU, see *Using the Adaptor Manager Administration Utility*).

Chapter 4. Processing using rules that refer to External Models

This chapter explains the appearance and behaviour of the LPS-Adaptor application during processing.

4.1 Processing

You can enter a compound and initiate processing as normal. If there are any Absolute reasoning rules that are active (enabled) and where the relevant processing constraint is "on", the program will attempt to resolve the rules by obtaining information from the relevant External Models.

4.1.1 User Input

If you have ticked the **Prompt user for Value** tick box in the processing constraints form and the program is unable to obtain the Physico-Chemical Property value from either the SD file or from an External Model, the User Input box will be displayed to allow you to enter a value. This is described further in *Changing Processing constraints for External Models*.

4.1.2 Error Handling

During processing using External Models, a variety of problems can occur, as the program must call several other applications including third-party applications, often over a network. In order to inform you of any problems, a status message is returned along with the results from the External Model. Error messages are not displayed on screen during processing as this would be annoying for the user, however during interactive processing, you can make use of the **Prompt user for Value** processing constraint to obtain early information about problems with obtaining Physico-Chemical Property values.

If no problems are encountered then the status string will be empty and will not be seen, however, if at any stage of obtaining the Physico-Chemical Property value and problem is encountered which stops the system from finding a value, the rule will evaluate to "OPEN" and the status string will be presented alongside any return value, on screen and in reports. In the Phase2 version of the program this is accompanied by further information from the External Model in the form of a list of properties and their values. This information is also shown in reports and on screen. For more information about Status messages see *The External Model Test Button*.

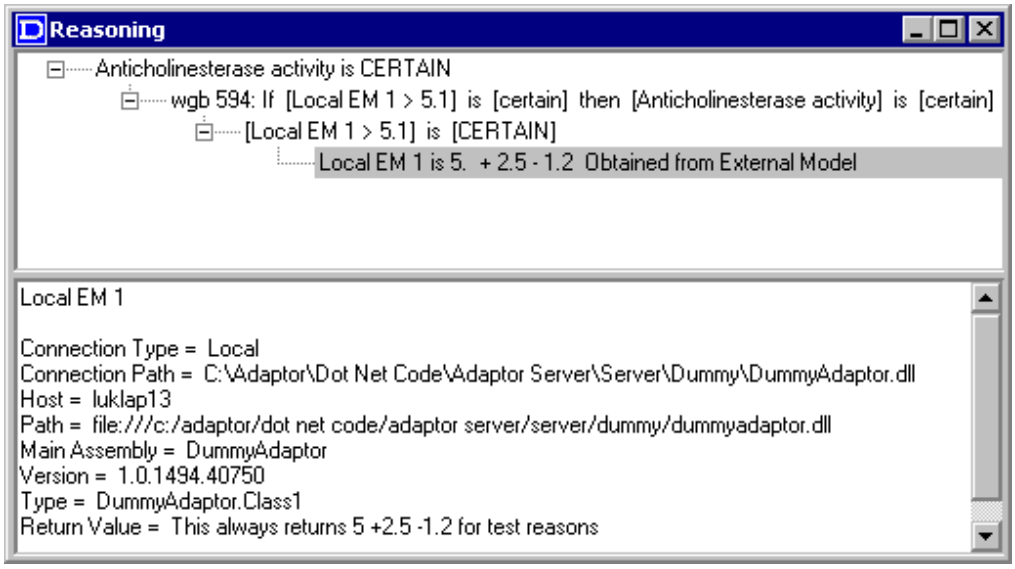
4.1.3 Tolerance

Some External Models supply a measure of *tolerance*. For example ACD LogP might supply a result of 3.1 +/- 0.25 to suggest that the value lies between 2.85 and 3.35. Other External Models may provide *asymmetrical tolerances* where the positive and negative tolerances are not equal, for example '4.2 + 0.8 – 1.0' would indicate that the value lies between 3.2 and 5.0. The LPS_Adaptor program takes measures of tolerance into account during reasoning if they have been supplied by an External Model or if they are included in the value obtained from an SD file. This is demonstrated in the figure below. Absolute Reasoning rule number 594 is asking if the value of *'Local EM 1'* is greater than 5.1. In the highlighted line we can see that the raw result value is 5.0 however when the tolerance values are taken into account the range for this value is between 3.8 and 7.5 so the Rule is satisfied.

4.2 Onscreen Results display

The results are displayed on screen as usual, however if you click the line containing the Physico-Chemical Property value on the Reasoning tree, further information from the External Model will be displayed in the comments field below the reasoning tree. This is shown in the diagram below for a Physico-Chemical Property called “Local EM 1”

Figure 10



These results can be used to create RTF, TXT or Modified SD file reports and can be saved to DRK files as usual.

4.3 Reports

In this version of LPS, more information is supplied to DEREK for Windows along with the Physico-Chemical Property value. This is in the form of a list of property-value pairs. This information is now included in the various reports that DEREK for Windows can produce. If any problems are encountered when attempting to obtain Physico-Chemical Property values from External Models this will be apparent in the report. The system reports information about Physico-Chemical Properties only if they are referred to by Absolute Reasoning Rules.

4.3.1 RTF Reports

An extract from an RTF report is shown below. It shows a list of Physico-Chemical Properties (starting with "ACD LogD" and their values for an oddly named compound "METEOR". Where values could not be obtained, this is indicated on the same line as the Physico-Chemical Property name and further explanation will usually be found in the information given below each Physico-Chemical Property.

The phrase "Unknown value" is displayed for dba-mouse and several other Physico-Chemical Properties. This indicates that there are Absolute Reasoning rules that refer to this Physico-Chemical Property but the processing constraints are set to disable both "input from SD file" and "input from External Model". Also the user chose "Cancel" when presented with the User Input box.

There are no new reporting options associated with this.

Figure 11

Compound Name:	METEOR
ACD LogD:	3.2 User entered
dba-mouse:	Unknown value
dba-rat:	Unknown value
DT1:	Unknown value
DT11:	Unknown value
Local EM 1:	5. +2.5 - 1.2 Obtained from External Model
Connection Type =	Local
Connection Path =	C:\Adaptor\Dot Net Code\Adaptor Server\Server\Dummy\DummyAdaptor.dll
Host =	luklap13
Path =	file:///c:/adaptor/dot net code/adaptor server/server/dummy/dummyadaptor.dll
Main Assembly =	DummyAdaptor
Version =	1.0.1494.40750
Type =	DummyAdaptor.Class1
Return Value =	This always returns 5 +2.5 -1.2 for test reasons
Local EM 2:	Unknown value External Model is not available
Connection Type =	Local
Connection Path =	C:\Adaptor\Dot Net Code\Adaptor Server\Server\Dummy\DummyAdaptor.dll
Host =	luklap13
Path =	file:///c:/adaptor/dot net code/adaptor server/server/dummy/dummyadaptor.dll
Main Assembly =	DummyAdaptor
Version =	1.0.1494.40750
Type =	DummyAdaptor.Class1
Error =	This always fails for test reasons
Log Kp:	-2.472 Calculated by the Potts & Guy equation
Log P:	1.416 Calculated by the Moriguchi estimation
Molecular Weight:	124.139 Calculated by LPS
pKa:	Unknown value
Remote EM 2:	Unknown value External Model is not available
Connection Type =	Remote
Connection Path =	TCP://localhost:9000/PCPService
Error =	Test failed with error: No connection could be made because the target machine actively refused it

4.3.2 TXT Reports

Note that in text reports the External Model details are all on one line, so like the SuperEndpoints they continue past the right hand edge of this screenshot.

Figure 12

```
Date Created: 09 February 2004
Version:      6.4.1
Database:     C:\Test Files\Test Databases\Copy of Dfw6 Adaptor.mdb
Database Version:    DFW6.0.0_2002_07_18
Testing Against:     All Alerts
Species:      bacterium     guinea pig    human  mammal
SuperEndpoints:             Carcinogenicity      Irritation    Miscellaneous endpoints     Mutagenicit
Consider Tautomers:  True
Hydrogen Options:    Perceive implicit and explicit hydrogens
Override automatic Log P calculation:     False
AutoSave:     Off
AutoSave Directory:  \

  METEOR      Lhasa Predictions
  METEOR      Carcinogenicity, bacterium  IMPOSSIBLE
  METEOR      Carcinogenicity, guinea pig PLAUSIBLE
  METEOR      Carcinogenicity, human      EQUIVOCAL
  METEOR      Carcinogenicity, mammal     EQUIVOCAL
  METEOR      Carcinogenicity, 252, 4-Alkylether phenol, 1 occurence.
  METEOR      Skin sensitisation, bacterium      IMPOSSIBLE
  METEOR      Skin sensitisation, guinea pig     PLAUSIBLE
  METEOR      Skin sensitisation, human   PLAUSIBLE
  METEOR      Skin sensitisation, mammal  PLAUSIBLE
  METEOR      Skin sensitisation, 417, Hydroquinone or precursor, 1 occurence.
  METEOR      Anticholinesterase activity, bacterium    CERTAIN
  METEOR      Anticholinesterase activity, guinea pig   CERTAIN
  METEOR      Anticholinesterase activity, human CERTAIN
  METEOR      Anticholinesterase activity, mammal       CERTAIN
  METEOR      Custom Predictions
  METEOR      Nothing to report
  METEOR      ACD LogD = 3.2  User entered
  METEOR      dba-mouse = Unknown value
  METEOR      dba-rat = Unknown value
  METEOR      DT1 = Unknown value
  METEOR      DT11 = Unknown value
  METEOR      Local EM 1 = 5.  + 2.5 - 1.2  Obtained from External Model    Connection Type=Local
  METEOR      Local EM 2 = Unknown value  External Model is not available   Connection Type=Local
  METEOR      Log Kp = -2.472  Calculated by the Potts & Guy equation
  METEOR      Log P = 1.416  Calculated by the Moriguchi estimation
  METEOR      Molecular Weight = 124.139  Calculated by LPS
  METEOR      pKa = Unknown value
  METEOR      Remote EM 2 = Unknown value  External Model is not available  Connection Type=Remote
```

4.3.3 Modified SD files

The text below shows an extract from a Modified SD file for the same compound as before (although when processed this time no value for ACD LogD was entered by the user).

Figure 13

```
> <AutoSave Directory>
\

> <ACD LogD>
Unknown value

> <dba-mouse>
Unknown value

…
> <Local EM 1>
5.  + 2.5 - 1.2  Obtained from External Model
Connection Type=Local
Connection Path=C:\Adaptor\Dot Net Code\Adaptor Server\Server\Dummy\DummyAdaptor.dll
Host=luklap13
Path=file:///c:/adaptor/dot net code/adaptor server/server/dummy/dummyadaptor.dll
Main Assembly=DummyAdaptor
Version=1.0.1494.40750
Type=DummyAdaptor.Class1
Return Value=This always returns 5 +2.5 -1.2 for test reasons

> <Local EM 2>
Unknown value  External Model is not available
Connection Type=Local
Connection Path=C:\Adaptor\Dot Net Code\Adaptor Server\Server\Dummy\DummyAdaptor.dll
Host=luklap13
Path=file:///c:/adaptor/dot net code/adaptor server/server/dummy/dummyadaptor.dll
Main Assembly=DummyAdaptor
Version=1.0.1494.40750
Type=DummyAdaptor.Class1
Error=This always fails for test reasons

> <Log Kp>
-2.472  Calculated by the Potts & Guy equation
```

Administering LPS_Adaptor

Contents

Installation Overview.

This document explains how to install the components necessary for using *LPS_Adaptor.*

You may also wish to refer to the following documents:

Document	Contents
Adaptor User Guide	Background information about LPS_Adaptor, including definitions of terms and a diagram and explanation of the components involved.
Using the Adaptor Manager Administration Utility	Explains how to create and edit Adaptor Lookup Files using the *Adaptor Manager Administration Utility*
How to write Adaptors for LPS	Information about writing custom Adaptors

Note: Before attempting Installation you should be familiar with the contents of the Adaptor User Guide.

Hardware and Software Requirements

The hardware and software requirements for *LPS_Adaptor* are the same as those described in *DEREK for Windows*.

It is possible to install *LPS_Adaptor* on a computer that already has an installation of LPS6 or LPS7, although it is not a requirement that one of these is installed.

Note: LPS_Adaptor should not be run at the same time as another copy of LPS as this could cause incorrect operation.

Installation Possibilities

The LPS_Adaptor application can be operated in a variety of configurations. If the LPS_Adaptor and the External Models are installed on the same machine it can be operated on a stand-alone basis or you may choose to install some of the components centrally so that the configuration files and External Models can be shared across users.

To Install LPS_Adaptor for stand-alone use, refer to the section *Installing LPS_Adaptor on a stand-alone machine*.

Installing a Multi-user Set-up.

Client machines in a Multi-user Set-up need only to have LPS_Adaptor installed (see *Installing LPS_Adaptor).* The Adaptor Host service, AMAU, Adaptors and External models are installed on one or more machines to which the client machines have access.

Note: LPS_Adaptor is not a client-server application, however the Adaptor host service allows Adaptors and External Models to be accessed by several LPS_Adaptor clients simultaneously (assuming that the External Model supports multiple access.)

The following sequence shows the typical procedure an Administrator must perform in order to set up a multi-user configuration of LPS_Adaptor. Some steps will require Administrator access rights.

1. Ensure that all client machines have LPS_Adaptor installed (see Installing LPS_Adaptor).
2. Install the *Adaptor Host Service* on a machine that users have access to.
3. Install any *Adaptors* that will be required. These must be installed in subdirectories of the *Adaptor Host Service.*

4. Install any *External Models* that are required if these have not been installed as part of the *Adaptor* installation. *External Models* do not necessarily have to be installed on the same machine as the *Adaptors*; this is specific to each *Adaptor*. See the *Adaptor's* own documentation for further details.

5. Install a copy of the AMAU on your own machine. Refer to the section *Installing the Adaptor Manager Administration Utility*.

6. Use the AMAU to create an *Adaptor Lookup File* that links the *Adaptors* to the names of Physico-Chemical Properties records in the DfW knowledgebase.

7. Save the Adaptor Lookup File to a location that can be accessed by all users of LPS_Adaptor. Users do not need write access to this directory.

8. Inform client users of the path and file name of the Adaptor Lookup File. They should run LPS_Adaptor and open the Processing constraints form. This value must then be entered in the *Adaptor Lookup File* text box on the *Phys-Chem Properties* tab.

9. Users of DfW will now be able to make use of the External Models, assuming appropriate Physico-Chemical Property Records and Rules have been written in the DfW knowledgebase.

Note: The *Name* value in the *Adaptor Lookup File* must match the *Name* value of the *Physico-Chemical Property Record*. If the Physico-Chemical Property names are not known at the time of writing the Adaptor Lookup File they can be altered in the Adaptor Lookup File later.

It is also possible to allow users to work more flexibly and to be able to choose between using shared External Models and using other External Models that may be locally installed. To allow client user to choose between External Models, client users must also install the AMAU, in addition to LPS_Adaptor. To make use of locally installed External Models the appropriate adaptors must be installed.

Installing LPS_Adaptor

This section explains how the *LPS_Adaptor* program can be installed on client machine.

The installation procedure for *LPS_Adaptor* is the same as the procedure described in *DEREK for Windows* except for the following:

- The *Microsoft .NET framework 1.1* must be installed.

  There are several methods of obtaining this:

  i. If you have access to the Internet then Microsoft .NET framework 1.1 can be downloaded and installed whilst installing Adaptor Manager. You may have to restart the installation of the Adaptor Manager after the .NET framework has been installed.

  ii. A copy of Microsoft .NET framework 1.1 is supplied with the LPS_Adaptor administrator disc, for further information about this contact your administrator. (The file is called dotnetfx.exe)

  iii. Microsoft .NET framework 1.1 is installed as part of the AMAU installation.

- The *Adaptor Manager* must be installed. This can be achieved by running the program *Adaptor Manager.msi* that can be found on the *LPS_Adaptor* installation disc.
  The *Adaptor Manager* is an essential component of the LPS_Adaptor application. It has no user interface other than that provided by LPS_Adaptor and cannot be accessed separately. It is not referred to elsewhere in the LPS_Adaptor documentation.

- By default, the software will be installed in the directory:

  ```
  C:\Program Files\Lhasa Ltd\LPS 651
  ```

- The program will be added to the start menu under **Start | Programs | Lhasa Ltd | LPS651**.

Note: It is particularly important to check the **README.TXT** file for last-minute information about installation.

Removing LPS_Adaptor

LPS_Adaptor can be removed from your machine by selecting *Add/Remove Programs* from the Windows Control Panel and removing both *Temp Adaptor Manager* and LPS *651*.

Installing LPS_Adaptor on a stand-alone machine.

This section describes how to set up *LPS_Adaptor* when all of the components will be installed locally. You may want to do this if you want to connect to External Models that are on the local machine.

1. Install the Adaptor Manager Installation Utility. Refer to the section Installing the Adaptor Manager Installation Utility below.
2. Install LPS_Adaptor as described in Installing LPS_Adaptor above.
3. Install Adaptors for the External Models.
4. Install any external models that you wish to use if these have not been previously installed.
5. Create an Adaptor Lookup File using the AMAU.

Removing a stand-alone installation of LPS_Adaptor.

A stand-alone installation of LPS_Adaptor can be removed by selecting *Add/Remove Programs* from the Windows Control Panel and removing the following components:

1. Any External Models that you no-longer wish to use, if these were installed along with LPS_Adaptor.
2. Any Adaptors for the External Models.
3. LPS_Adaptor (LPS 651).
4. The Adaptor Manager Installation Utility.

Installing the Adaptor Manager Administration Utility (AMAU).

The AMAU should be installed on the machine of any user who needs to create or edit Adaptor Lookup Files. It occupies approximately 160 kilobytes.

1. Insert the *Adaptor Manager Administration Utility* compact disc into your CD ROM drive.
2. If this disc does not Auto-run then browse to the setup.exe file and run (Open) it.
3. The installation program will guide you through the installation process. By default the AMAU will be installed to the directory *C:\Program Files\Lhasa Ltd\Adaptor Manager Admin Util* and a menu item will be added to the start menu (**Start Menu\Programs\Lhasa Ltd\Adaptor Manager Administration**).

Removing the Adaptor Manager Administration Utility (AMAU).

The *AMAU* can be removed from your machine by selecting *Add or Remove Programs* from the Windows *Control Panel* and removing *Adaptor Manager Admin Utility*.

Installing the Adaptor Host Service

The Adaptor Host Service should be installed on any machine that will host Adaptors for use by one or more users over a network. It occupies approximately 60 kilobytes of hard disk space.

Note: The Adaptor Host Service requires the .NET framework 1.1 to be installed. Refer to *Installing LPS_Adaptor* for further information about obtaining the .NET framework.

1. Insert the *Adaptor Host Service* compact disc into your CD ROM drive.
2. If this disc does not Auto-run then browse to the setup.exe file and run (Open) it.
3. The installation program will guide you through the installation process. By default the Adaptor Host Service is installed to the directory *C:\Program Files\Lhasa Ltd\Adaptor Server*. No menu item will be added to the start menu.
4. Open the Windows *Services* utility to manually start the service, which is called *Lhasa Adaptor Server*. The service is set to start Automatically when the machine boots up so this procedure only needs to be done once.

Note: The Adaptor Host Service is **not** required for stand-alone use, i.e. where Adaptors are accessed by only one LPS_Adaptor application, which is running on the same machine.

Removing the Adaptor Host Service

The *Adaptor Host Service* can be removed from your machine by selecting *Add or Remove Programs* from the Windows *Control Panel* and removing *Adaptor Server*.

Installing Adaptors

The current version of LPS_Adaptor is supplied with two Adaptors, one for ACD LogD and the other demonstrates a link to an Access database. For specific instructions about the installation of other Adaptors you should refer to the Adaptor documentation.

Generally speaking, Adaptors that are being hosted (by the Adaptor Host Service) should be installed to a sub-directory of the Adaptor Host directory. By Default this is *C:\Program Files\Lhasa Ltd\Adaptor Server*. For stand-alone use the directory to which Adaptors are installed is unimportant.

Note that adaptors installed here will be automatically hosted and will be available to users of LPS_Adaptor, assuming the *Adaptor Lookup File* has their details.

Installing the Database Adaptor

The Database Adaptor allows users to link to the Lois Gold database, which is included in the Database Adaptor installation.

It occupies approximately 1.37Mb of hard disk space.

1. Insert the *Database Adaptor* compact disc into your CD ROM drive.
2. If this disc does not Auto-run then browse to the setup.exe file and run (Open) it.
3. The installation program will guide you through the installation process. By default the *Database Adaptor* is installed to the directory *C:\Program Files\Lhasa Ltd\Adaptor Server\DB Adaptor*. No menu item is added to the start menu.

Configuring the Database Adaptor.

1. The Database Adaptor configuration file uses relative paths point to the database, so this should require no alteration. It is shown here for information only.

Figure 1, The Database Adaptor Configuration File

```
<Adapter>
  <Database>gold_data.MDB</Database>
  <PCP>
    <dba-mouse>
      <select>import.mouse</select>
    </dba-mouse>
    <dba-rat>
      <select>import.rat</select>
    </dba-rat>
  </PCP>
</Adapter>
```

2. Use the AMAU to create or edit the Adaptor Lookup File so that it links a Physico-Chemical Property name in the DfW knowledgebase with this Adaptor (DBAdaptor.dll). For details about how to do this refer to the document *Using the adaptor Manager Administration Utility*.

If relevant Physico-Chemical Properties and Rules have been entered into the DfW knowledgebase, the following steps can also be performed.

3. Run LPS_Adaptor and view the processing constraints. Check that the path of the Adaptor is shown in the *External Model* column of the grid on the *Phys-Chem Properties* tab.

4. Tick the *Enable External Model* tick box and then click the *Test External Models* button. This will display a report that will indicate the status of the currently enabled External Models.

5. If no problems are reported, you are ready to process using LPS_Adaptor.

Removing the Database Adaptor

The *Database Adaptor* can be removed from your machine by selecting *Add or Remove Programs* from the Windows *Control Panel* and removing *DB Adaptor (Temp).*

Installing the ACD LogD Adaptor

The *ACD LogD Adaptor* allows users to link to ACD's *ACD/LogD Batch* application in order to obtain values for LogD and LogP. It occupies approximately 50kb of hard disk space.

ACD/LogD Batch can be obtained from *Advanced Chemistry Development* (http://www.acdlabs.com/).

1. Insert the *ACD LogD Adaptor* compact disc into your CD ROM drive.

2. If this disc does not Auto-run then browse to the setup.exe file and run (Open) it.

3. The installation program will guide you through the installation process. By default the *ACD LogD Adaptor* is installed to the directory *C:\Program Files\Lhasa Ltd\Adaptor Server\ACD Adaptor*. No menu item is added to the start menu.

Configuring ACD LogD Adaptor.

The ACD LogD Adaptor configuration file must be edited to point to the ACD executable file *pchbat.exe* is installed.

1. Open ACD_Adaptor.DLL.config using a text editor such as *Notepad*.

Figure 2. ACD_Adaptor.DLL.config

```
<?xml version="1.0" encoding="utf-8" ?>
<configuration>
    <ACDCalc>
        <Executable path="C:\acd70\pchbat.exe"/>
        <Temp path="C:\temp"/>
        <Ph value="8.2"/>
    </ACDCalc>
</configuration>
```

2. Replace the existing *Executable path* value with the UNC path to the ACD executable file. In this example the existing path (which includes the file name) is 'C:\acd70\pchbat.exe'.

3. Alter the *Temp Path* if required. This is used by the Adaptor and by the External Model for writing temporary files.

Note: It is advisable to keep this path short as long path names could cause problems when communicating with the external model.

4. Alter the pH value if required.

5. Save your changes and close your text editor.

6. Use the AMAU to edit the Adaptor Lookup File so that it includes information about the ACD Adaptor. For details about how to do this refer to the document *Using the adaptor Manager Administration Utility*.

If relevant Physico-Chemical Properties and Rules have been entered into the DfW knowledgebase, the following steps can also be performed.

7. Run LPS_Adaptor and view the processing constraints. Check that the path and file name of the Adaptor is shown in the *External Model* column of the grid on the *Phys-Chem Properties* tab.
8. Tick the *Enable External Model* tick box and then click the *Test External Models* button. This will display a report, which will indicate the status of the currently enabled External Models.
9. If no problems are reported, you are ready to process using LPS_Adaptor.

Removing ACD LogD Adaptor

The *ACD LogD Adaptor* can be removed from your machine by selecting *Add or Remove Programs* from the Windows *Control Panel* and removing *ACD Adaptor*.

Installing External Models

For specific instructions about the installation of External Models you should refer to the External Models own documentation.